## REMARKS/ARGUMENTS

This is in response to the Office Communication dated November 8, 2005 noting that the Examiner believes the response of Applicants dated August 22, 2005 to be non-responsive. In particular, the Examiner has noted that the elected species (peptide PSM-P1) was canceled from the pending claims. Therefore, although Applicants believe the earlier filed response to be complete and fully responsive, claims 10, 14, 39 and 43 have been amended to reinsert the peptide PSM-P1 and the other peptides canceled from the claims. No new matter is added by the present amendments. Applicants also provide below additional comments addressing the rejections of the Examiner stated in the previous office action to reflect the inclusion of the prostate antigen specific peptides in certain of the pending dependent claims. Applicants request reconsideration of the claims in light of the above amendments and remarks below and in the prior response.

Rejections under 35 U.S.C. §103(a)

Claims 10-14, 16-21 and 36-43 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,788,963 (1998, IDS) in view of Thurnher *et al.* (1997, IDS) and Ramoner *et al.* (1998, IDS). The Examiner has cited the '963 patent as allegedly teaching " a method for producing an anti-tumor cell, antigen specific cytotoxic T cell (CTL) response comprising administering to a patient an effective amount of human DCs, said DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1 (SEQ ID NO:1) derived from various sources including tumor cell lysates and purified antigens." The Examiner also cites the '963 patent as allegedly teaching that the DCs are obtained from peripheral blood, have been cryopreserved, have been obtained from a healthy HLA matched donor, are extended life span, and can be administered to a metastatic prostate cancer patient. The Examiner believes that the reference differs from the claimed invention only in that it does not teach the use of BCG in the *in vitro* exposure of the DCs to antigen.

Thurnher *et al.* is cited by the Examiner as allegedly teaching the *in vitro* maturation and activation of DCs with BCG and that the reference further allegedly teaches that DCs matured in the presence of BCG may also take up tumor antigens and thus, then be capable of activating tumor-reactive T cells in a cytokine milieu that favors the generation of a strong anti-tumor CTL response. The Examiner also believes that the references teaches tumor-antigen loading of DCs cultured in BCG.

Ramoner *et al.* is cited by the Examiner as allegedly further extending the work of Thurnher *et al.* by teaching that BCG 'is a potent activator of human DCs' and allegedly teaching that BCG stimulates the ability of DCs to activate T cells. The Examiner also believes that the reference teaches the BCG could be used in DC based tumor immunotherapy.

The Examiner has combined the references to suggest that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method for producing an anti-tumor cell, antigen specific CTL response comprising administering to a patient an effective amount of human DCs, the DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1, the DCs having been obtained from peripheral blood, having been cryopreserved, having been obtained from a healthy HLA matched donor, having been extended life span, and having been administered to a metastatic prostate cancer patient, as taught by the '963 patent." It is further believed by the Examiner that "one of ordinary skill in the art would have been motivated to add BCG to the *in vitro* exposure of DCs to antigen for an improved anti-tumor, antigen specific CTL response, given the combined teachings of Thurnher *et al.* and Ramoner *et al.* that 1) BCG causes the maturation of DC and thus, the DCs are capable of activating tumor-reactive T cells in a cytokine milieu that favors the generation of a strong anti-tumor CTL response and 2) BCG 'is a potent activator of human DCs', BCG stimulates the ability of DCs to activate T cells, and BCG could be used in DC based tumor immunotherapy." The Examiner also believes that claims 36 and 40 "comprise only the routine optimization of the claimed method and fall well within the purview of one of ordinary skill in the art at the time of the invention."

Applicants do not agree with the Examiner's summary of the motivation provided by the art or with summary of what the skilled artisan would have considered *prima facie* obvious at the time of the claimed invention. Applicants do not believe that the Examiner has made a proper showing, but in order to further expedite prosecution of certain subject matter disclosed in the application the claims have been amended. In particular, claim 10 has been amended to recite that the human dendritic cells are "exposed *in vitro* to a soluble, exogenous tissue specific antigen and bacillus Calmette Guerin (BCG) or BCG with lipopolysaccharide (LPS) to induce antigen processing and to promote Major Histocompatibility Complex- (MHC-) class I presentation of the antigen." By this amendment the claim more distinctly recites that the antigen is a soluble, exogenous tissue specific antigen that can be processed within the cell prior to presentation in the context of MHC-class I. Peptides, like larger soluble polypeptides and proteins, can be taken up by DCs, and although they do not necessarily require processing by the dendritic cell prior to presentation, peptides having the amino acid sequences recited in claims 14, 39 and 43 can be processed and associated with MHC-class I molecules using the methods of the present invention. The '963 patent as summarized by the Examiner does not disclose or suggest the methods of compositions of the pending claims to promote Major Histocompatibility Complex- (MHC-) class I presentation of the antigen either alone or in any combination with the other references cited.

It should also be noted that Applicants do not believe that Thurnher *et al* disclose *in vitro* exposure of DCs to BCG provides a cytokine milieu that favors the generation of a strong anti-tumor CTL response. The passage referred to by the Examiner appears to suggest that the cytokine milieu is induced *in vivo* by the uptake of tumor antigens along with BCG as a consequence of the intra- or peri-tumoral administration of BCG. This would suggest instead of *in vitro* conditions conducive to the induction of the claims response that *in vivo* administration of BCG with a tumor antigen would provide the cytokine milieu that favors the generation of a strong anti-tumor CTL response.

Further, Applicants do not believe that claims 36 and 40 merely comprise routine optimization. In particular, the uptake of soluble, exogenous antigen by DCs subsequent to

activation and maturation is contrary to the teachings of the art. See page 32, lines 18 through 29 of the specification. The art discloses that exogenous soluble antigen is processed in the MHC class II pathway and cellular antigens, such as bacteria and virus, are processed by the MHC class I pathway for presentation on the surface of DCs. The art further teaches that mature DCs typically do not take up and process antigen, while the present application demonstrates that sufficient soluble antigen is taken up and processed by mature DCs to increase the expression of mature DC surface markers including CD8.

Therefore, Applicants do not believe that claims 10-14, 16-21 and 36-43 as amended and in view of the remarks above are unpatentable over U.S. Patent 5,788,963 in view of Thurnher *et al.* and Ramoner *et al.* and reconsideration of the claims and withdrawal of the rejection by the Examiner is respectfully requested.

Rejections under 35 U.S.C. §112

Claims 36 through 43 stand rejected under 35 U.S.C. §112, first paragraph, the Examiner believing that the specification does not contain written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. In particular, the Examiner does not believe that the specification and the claims as originally filed provide support for the generic invention as recited in claims 36 and 40.

Applicants traverse this ground of rejection. In particular, support for independent claim 36 can be found throughout the specification. See for example, page 5, lines 23-25, page 10, lines 11-15, and 19-22, page 18, lines 11-32, and the Examples. Support for independent claim 40 is explicitly recited in Example 2. As a particular embodiment of the broader concept of the invention includes simultaneous exposure of the DC with antigen and BCG, and the example describes a model system, Applicants believe that the use of any soluble exogenous tissue associate antigen will provide a similar result. As independent claims 36 and 40 drawn to a generic antigen are believed to be sufficiently described in the specification and

claims as filed reconsideration of the rejection of claims 36 to 43 under 35 U.S.C. §112, first paragraph is respectfully requested.

## CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

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